

**Amendment and Response**

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Applicant(s): Dominic COSGROVE

Serial No.: 10/698,121

Filed: 31 October 2003

For: INDUCIBLE LIGAND FOR  $\alpha 1 \beta 1$  INTEGRIN AND USES**Amendments to the Claims**

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

**Listing of Claims**

1. (Currently amended) A method of treating a patient having a chronic inflammatory disease associated with the interaction of Collagen XIII with  $\alpha 1 \beta 1$  integrin positive monocytes, the method comprising administering to the patient ~~a blocking agent to neutralize the capacity of an antibody to Collagen XIII, wherein the antibody reduces the rate of efflux of Collagen XIII to bind to a  $\alpha 1 \beta 1$  integrin positive monocytes into the interstitial space at the site of inflammation.~~
2. (Currently amended) The method of claim 1 wherein the chronic inflammatory disease is characterized by progressive pathogenesis resulting from infiltrating monocytes, ~~lymphocytes, or both.~~
3. (Currently amended) The method of claim 1 wherein the chronic inflammatory disease is renal fibrosis, ~~lung fibrosis, liver fibrosis, rheumatoid arthritis, psoriasis, colitis, or crescentic glomerulonephritis.~~
4. (Cancel)
5. (Currently amended) The method of claim 1 wherein the ~~blocking agent~~ antibody is a ~~neutralizing monoclonal~~ antibody.
6. (Currently amended) The method of claim 1 wherein the ~~blocking agent~~ antibody blocks the interaction of  $\alpha 1 \beta 1$  integrin on peripheral blood monocytes ~~and/or lymphocytes~~ with Collagen XIII on vascular endothelium of chronically inflamed tissues.

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7. (Currently Amended) A method for treating a subject having an inflammatory disease or other condition where integrin  $\alpha 1\beta 1$ -positive interstitial monocyte and/or lymphocyte accumulation is observed, the method comprising administering to the subject an active agent antibody to Collagen XIII that ~~disrupts~~ disrupts the interaction between Collagen XIII and  $\alpha 1\beta 1$  integrin.
8. (Currently amended) The method of claim 7 wherein the ~~active agent~~ antibody to Collagen XIII blocks binding of Collagen XIII and  $\alpha 1\beta 1$  integrin.
9. (Cancel)
10. (Currently amended) The method of claim [[8]] 7 wherein the ~~blocking agent is an antibody~~ is a monoclonal antibody.
11. (Currently amended) The method of claim 7 wherein the inflammatory disease or other condition is renal fibrosis, ~~lung fibrosis, liver fibrosis, rheumatoid arthritis, psoriasis, colitis, or crescentic glomerulonephritis.~~
12. (Currently amended) The method of claim 7 wherein the ~~active agent~~ antibody blocks the interaction of  $\alpha 1\beta 1$  integrin on peripheral blood monocytes and/or lymphocytes with Collagen XIII on vascular endothelium of chronically inflamed tissues.
13. (Currently amended) A method of reducing selective efflux of integrin  $\alpha 1\beta 1$ -positive monocytes into the interstitium of chronically inflamed tissues, the method comprising contacting the  $\alpha 1\beta 1$  integrin on peripheral blood monocytes and/or lymphocytes with an ~~active agent~~ an antibody to Collagen XIII that interferes with the interaction between Collagen XIII and  $\alpha 1\beta 1$  integrin.

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14. (Cancel)

15. (Currently amended) The method of claim 13 wherein ~~reducing selective efflux of integrin  $\alpha$ 1 $\beta$ 1-positive monocytes into the interstitium of chronically inflamed tissues comprises contacting an~~ the antibody blocks that binds to the interaction of  $\alpha$ 1 $\beta$ 1 integrin on peripheral blood monocytes with Collagen XIII ligand on the cell surface of the vascular/capillary endothelial cells of inflamed tissues ~~under conditions effective to block the binding site for Collagen XIII.~~

16. (Cancel)

17. (Currently amended) A method of reducing the rate of monocyte and/or lymphocyte efflux into the interstitial space of chronically inflamed tissues, the method comprising contacting the tissue with an antibody to Collagen XIII wherein the antibody blocks blocking Collagen XIII from binding with  $\alpha$ 1 $\beta$ 1 integrin.

18-20. (Cancel)

21. (Currently amended) The method of claim 17 wherein ~~blocking comprises contacting the Collagen XIII ligand with a mono-specific antibody~~ is a monoclonal antibody.

22. (Cancel)

23. (Currently amended) A method of blocking the interaction of  $\alpha$ 1 $\beta$ 1 integrin on peripheral blood monocytes ~~and/or lymphocytes~~ with Collagen XIII on vascular endothelium of chronically inflamed tissues, the method comprising contacting the monocytes ~~and/or lymphocytes~~, the vascular endothelium, or both with an ~~agent that either occupies the Collagen XIII binding site on  $\alpha$ 1 $\beta$ 1 integrin or blocks the  $\alpha$ 1 $\beta$ 1 binding site on~~ an antibody to Collagen XIII.

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24. (Cancel)

25. (Currently amended) The method of claim 23 wherein the ~~agent that blocks the  $\alpha 1\beta 1$  binding site on Collagen XIII~~ antibody is a neutralizing monoclonal antibody.

26. (Cancel)

27. (Currently amended) The method of claim [[26]] 1 wherein the ~~agent~~ antibody inhibits binding of Alexa-conjugated purified  $\alpha 1\beta 1$  integrin to MCP-1 treated primary endothelial cells.

28. (Currently amended) The method of claim [[26]] 7 wherein the ~~agent is an antibody that blocks~~ inhibits the interaction binding of Alexa-conjugated purified  $\alpha 1\beta 1$  integrin to MCP-1-treated vascular endothelial cells in culture.

29-42. (Cancel)

43. (New) A method of treating a patient having a kidney disease associated with an accumulation of  $\alpha 1\beta 1$  integrin positive monocytes in the interstitium, the method comprising administering to the patient an antibody to Collagen XIII, wherein the antibody reduces the rate of efflux of  $\alpha 1\beta 1$  integrin positive monocytes into the renal interstitium.

44. (New) A method of treating a patient having a progressive renal fibrosis, the method comprising administering to the patient an antibody to Collagen XIII, wherein the antibody prevents the binding of Collagen XIII to  $\alpha 1\beta 1$  integrin positive monocytes.

45. (New) The method of claim 13 wherein the antibody is a monoclonal antibody.

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46. (New) The method of claim 17 wherein the antibody blocks the interaction of  $\alpha 1\beta 1$  integrin on peripheral blood monocytes with Collagen XIII on vascular endothelium of chronically inflamed tissues.
47. (New) The method of claim 23 wherein the antibody blocks the interaction of  $\alpha 1\beta 1$  integrin on peripheral blood monocytes with Collagen XIII on vascular endothelium of chronically inflamed tissues.
48. (New) The method of claim 13 wherein the antibody inhibits binding of Alexa-conjugated purified  $\alpha 1\beta 1$  integrin to MCP-1 treated primary endothelial cells.
49. (New) The method of claim 17 wherein the antibody inhibits binding of Alexa-conjugated purified  $\alpha 1\beta 1$  integrin to MCP-1 treated primary endothelial cells.
50. (New) The method of claim 23 wherein the antibody inhibits binding of Alexa-conjugated purified  $\alpha 1\beta 1$  integrin to MCP-1 treated primary endothelial cells.
51. (New) The method of claim 43 wherein the antibody inhibits binding of Alexa-conjugated purified  $\alpha 1\beta 1$  integrin to MCP-1 treated primary endothelial cells.
52. (New) The method of claim 44 wherein the antibody inhibits binding of Alexa-conjugated purified  $\alpha 1\beta 1$  integrin to MCP-1 treated primary endothelial cells.
53. (New) The method of claim 1 wherein the antibody binds to SEQ ID NO:1.
54. (New) The method of claim 7 wherein the antibody binds to SEQ ID NO:1.
55. (New) The method of claim 13 wherein the antibody binds to SEQ ID NO:1.

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56. (New) The method of claim 17 wherein the antibody binds to SEQ ID NO:1.
57. (New) The method of claim 23 wherein the antibody binds to SEQ ID NO:1.
58. (New) The method of claim 43 wherein the antibody binds to SEQ ID NO:1
59. (New) The method of claim 44 wherein the antibody binds to SEQ ID NO:1
60. (New) The method of claim 1 wherein the antibody binds to SEQ ID NO:2.
61. (New) The method of claim 7 wherein the antibody binds to SEQ ID NO:2.
62. (New) The method of claim 13 wherein the antibody binds to SEQ ID NO:2.
63. (New) The method of claim 17 wherein the antibody binds to SEQ ID NO:2.
64. (New) The method of claim 23 wherein the antibody binds to SEQ ID NO:2.
65. (New) The method of claim 43 wherein the antibody binds to SEQ ID NO:2
66. (New) The method of claim 44 wherein the antibody binds to SEQ ID NO:2